SPS Medication Safety Update
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Observatory of recent safe medication practice research, reports, and publications

Presented by

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Recent regulator and statutory body activity

NHS Improvement

National Patient Safety Alert

Use of oxygen cylinders where patients do not have access to medical gas pipeline systems

- During periods of extreme pressure, often exacerbated by a surge in respiratory conditions, the demand for oxygen cylinders, in particular the small cylinders, increases in the NHS. This surge in demand increases the known risks associated with the use of medical gas cylinders, and introduces new risks, across three main areas:
  - patient safety
  - fire safety
  - physical safety.
- NHS England has issued providers with a summary of best practice guidance on the 'Safe use of oxygen cylinders' to help NHS organisations to prevent these risks.

UKMi UK Medicines Information | Specialist Pharmacy Service | MHRA | NHS England

Recent regulator and statutory body activity

MHRA

Class 2 Medicines Recall: UCB Pharma Ltd, Dioctyl 100 mg Capsules, EL (23)A/02

- UCB Pharma Ltd is recalling one batch of Dioctyl 100 mg Capsules as a precautionary measure due to the presence of a foreign capsule being found in a sealed pack.

Class 4 Medicines Defect Information: Morningside Healthcare Limited, Hyoscine Butylbromide 20 mg Film-coated Tablets, EL (22)A/48

- Affected batches may contain a PIL for Midodrine Hydrochloride 2.5 mg & 5 mg Tablets. There is no risk to product quality and efficacy, but healthcare professionals are advised to check and provide a copy of the correct PIL.

Class 4 Medicines Defect Information: Lucis Pharma Ltd, Oxycodone Hydrochloride 10mg/ml oral solution, EL (22)A/49

- Lucis Pharma Ltd have announced a typographical error in text on the rear side of the outer packaging which incorrectly states that: ‘Each 1ml of oxycodone hydrochloride oral solution contains 1mg of oxycodone hydrochloride.’ The correct text should state ‘10mg of oxycodone’.

Class 4 Medicines Defect Information: ADVANZ PHARMA, MacroBID 100mg Prolonged-Release Capsules, EL (22)A/50

- Specified batches have been packed with incorrect Patient Information Leaflet, missing important safety information of possible side effects (scarring due to lung tissue, rare cases of fatal liver failure & bone marrow damage leading to anaemia) & minor editorial inconsistencies.

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Recent regulator and statutory body activity

MHRA

Class 4 Medicines Defect Information: Galderma (U.K.) Limited, Etrivex 500 micrograms/g Shampoo, EL (22)A/51

- Specified batches of Etrivex Shampoo (0114252, 0114277 [both expiry 07/23] & 0114291 expiry 04/2023) have been packaged with patient information leaflets missing safety information and adverse effect of blurred vision (unknown frequency).

Class 4 Medicines Defect Information: Albireo AB, Bylvay (odevixibat) 1200 micrograms Hard Capsules, EL (23)A/01

- The side panel of the bottle label of a certain batch of Bylvay 1200 micrograms Capsules erroneously reflect the content of the active ingredient as 400 micrograms odevixibat. There is no risk to product quality and efficacy, therefore the affected batch is not being recalled

Class 4 Medicines Defect Information: Galderma (U.K.) Limited, Epiduo 0.1% / 2.5% gel (45 g), EL (22)A/52

- Galderma (U.K.) Limited has informed the MHRA that the Patient Information Leaflet (PIL) packaged in some batches of Epiduo 0.1% / 2.5% gel contain outdated safety information regarding pregnancy.

Company led medicines recall: Mawdsley-Brooks & Company Limited, Fluphenazin-neuraxpharm® D 25 & 100 mg/ml Solution for Injection, CLMR(23)A/01

- Specific batches of the product are recalled as a precautionary measure due to validation tests demonstrating the leaching of filter additives that are above the acceptable limit.

Recent regulator and statutory body activity

MHRA

Drug Safety Update

Valproate: reminder of current Pregnancy Prevention Programme requirements; information on new safety measures to be introduced in the coming months

- In view of data showing ongoing exposure to valproate in pregnancy, this alert reminds HCPs of the risks in pregnancy, current Pregnancy Prevention Programme requirements and the new safety measures being put into place in the coming months following advice from CHM.
- The CHM has advised that no one under the age of 55 should be initiated on valproate unless two specialists independently consider and document that there is no other effective or tolerated treatment.

Dupilumab (Dupixent▼): risk of ocular adverse reactions and need for prompt management

- Healthcare professionals prescribing dupilumab should be alert to the risks of ocular reactions. New onset or worsening ocular symptoms require prompt review. Referral for ophthalmological examination should be made as appropriate.

Pharmacovigilance Risk Assessment Committee (PRAC)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PRAC recommends withdrawal of pholcodine medicines from EU market

- Data found use of pholcodine within 12 months of general anaesthesia is a risk factor for developing an anaphylactic reaction to neuromuscular blocking agents. As it was not possible to identify measures to minimise the risk, the market authorisation is being withdrawn in the EU.

EMA's safety committee PRAC recommends alignment of dose recommendations for Janus kinase (JAK) inhibitors used to treat several chronic inflammatory disorders in patients with certain risk factors

- European PRAC has further reviewed measures to minimise the risk of serious side effects associated with JAK inhibitors, and has recommended use of a lower dose of baricitinib for patients at higher risk of blood clots, CV conditions and cancer.

European PRAC discusses direct healthcare professional communication (DHPC) regarding fatal cases of acute liver failure reported in patients treated with onasemnogene abeparvovec

- The DHPC informs healthcare professionals of these reported cases, and of resulting updated recommendations for monitoring liver function, assessing suspected liver injury after infusion, and further advice regarding tapering the corticosteroid treatment.

Direct HCP communication

Januvia® 100 mg film-coated tablets (Sitagliptin) - Temporary supply of Januvia® 100 mg film-coated tablets in German language packs

- To resolve a temporary issue in supply, a number of batches originally destined for Germany have been repurposed for Great Britain and are expected to be on the market from early January 2023. The English patient information leaflet should be downloaded and supplied.

Nulojix – risk of medication errors due to change in maintenance dose from 5 mg/kg to 6 mg/kg

- With the implementation of a new manufacturing process, the maintenance dose for Nulojix (belatacept) will be changed to 6 mg/kg every 4 weeks. For ~1-2 months starting October 2022, Nulojix from both the previous and new manufacturing processes will coexist on the market.

Imbruvica (ibrutinib): New risk minimisation measures, including dose modification recommendations, due to the increased risk for serious cardiac events

- Prior to initiating ibrutinib, clinical evaluation of cardiac history and function should be performed.
- In patients with risk factors for cardiac events, benefits and risks should be assessed before initiating treatment with Imbruvica; alternative treatment may be considered.
- Ibrutinib should be withheld for any new onset or worsening grade 2 cardiac failure or grade 3 cardiac arrhythmias.

Manufacturer RMM or SPC changes

Revised SPC: Deximune (ciclosporin) 50 mg soft capsules

- SPC updated to note hearing impairment has been reported in the post-marketing phase in patients with high levels of ciclosporin.

Revised SPC: Moviprep (macrogol 3350) powder for oral solution- all presentations

- The warning that medicinal products taken orally one hour before, during and one hour after Moviprep administration may be flushed from the gastrointestinal tract unabsorbed now includes oral contraceptive pill as an example.

RMM: Educational Risk Minimisation Material: Brinavess (vernakalant) pre-infusion checklist

- Prior to administration, the prescriber is asked to determine eligibility of the patient through use of this checklist (supplied with the product). The checklist should be placed on the infusion container to be read by the healthcare professional involved in its administration.

RMM: Checklist for healthcare professionals prescribing glycopyrronium bromide oral solution

- A checklist is provided to support healthcare professionals mitigate the risk that patients prescribed this medicine will experience anticholinergic side effects. A reminder card for patients is also available providing advice on how to manage common side effects.

Drug discontinuations

Discontinuation of Itraconazole (Sporanox) 100mg capsules

- Generic itraconazole 100mg capsules remain available.

Discontinuation of Dalteparin sodium 10,000units/1ml solution for injection ampoules

- Based on forecasted UK demand, stock will be exhausted by May 2023.
- Alternative strengths and formulations of dalteparin and other low molecular weight heparins remain available and will be able to support increased demand.

Discontinuation of Glyceryl trinitrate (Nitronal) 5mg/5ml solution for infusion ampoules

- Published 22 December 2022
- Patients can be switched from glyceryl trinitrate (Nitronal) 5mg/5ml solution for infusion ampoules to glyceryl trinitrate (Nitronal) 50mg/50ml solution for infusion vials.

Stemetil (Prochlorperazine mesilate) 5 mg / 5 ml Syrup: permanent discontinuation due to laboratory test results demonstrating excess levels of N-nitrosomethylphenylamine

- Stemetil 5 mg / 5 ml Syrup is being permanently discontinued in the UK from October 2022.

New drug shortages

Shortage of Norditropin (somatropin) Flexpro 10mg/1.5ml, 15mg/1.5ml and Norditropin (somatropin) NordiFlex 5mg/1.5ml, 10mg/1.5ml and 15mg/1.5ml solution

- Impact tier 2
- Anticipated re-supply 24th February
- Identify and clinically review all patients.
- Ensure that new patients are not initiated on Norditropin Flexpro or Norditropin NordiFlex for the full duration of 2023.
- Omnitrope (somatropin) SurePal 5mg/1.5ml, 10mg/1.5ml and 15mg/1.5ml solution for injection cartridges remain available and will be able to support a full increase in demand during this time.

Shortage of Estradiol (Estraderm MX) 75micrograms/24hours and 100micrograms/24hours transdermal patches

- Impact tier 2
- Anticipated re-supply 27th January
- An alternative brand of estradiol patches, Evorel, of the same strengths remain available and can support a full uplift in demand.
- Estradiol (Estraderm MX) 25micrograms/24hours transdermal patches and Estradiol (Estraderm MX) 50micrograms/24hours transdermal patches remain available.
- SPS article "Prescribing available HRT products"

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Current drug shortages - updates

Medicine	Updated re-supply date	Actions
Tapentadol 20mg/ml oral solution sugar free	Anticipated resupply date updated to 5th February 2023	Palexia 50mg tablets remain available.
Vecuronium bromide 10mg powder for solution for injection vials	Anticipated re-supply date updated to 30th January 2023	Rocuronium 50mg/5ml solution for injection vials and atracurium 50mg/5ml solution for injection ampoules remain available and can support an uplift in demand.
Calcichew 500mg chewable tablets	Anticipated re-supply date updated to 17 February 2023	Other calcium carbonate chewable tablets remain available
Chlordiazepoxide 5mg and 10mg capsules	Anticipated re-supply date for chlordiazepoxide 10mg capsules updated to 27th February 2023	Diazepam tablets are an alternative benzodiazepine option for treating alcohol withdrawal and suppliers can support an increase in demand.
Dulaglutide (Trulicity) 0.75mg, 1.5mg, 3mg and 4.5mg solution for injection devices	Anticipated re-supply date updated to 2nd April 2023	Consider alternative GLP-1 receptor agonists (RAs) until the shortage has resolved.
Lidocaine 1% and 2% with adrenaline 100micrograms/20ml	Anticipated re-supply date updated to 31st December 2023.	See SPS shortage tracker
Lidocaine 5% ointment	Anticipated re-supply date updated to 3rd Mar 2023	LMX4 (lidocaine 4% w/w) cream remains available.
Methylphenidate prolonged-release tablets	Updated to reflect resupply dates for OOS preparations	See SPS shortage tracker
Pethidine 50mg tablets	Anticipated re-supply date updated to 1st July 2023	Specialist importers have confirmed they can source unlicensed tablets
Prochlorperazine 12.5mg/1ml solution for injection ampoules	Anticipated re-supply date updated to 13th February 2023	Limited supplies remain available in NHS Trusts and health boards. Alternative anti-emetics remain available and are able to support an uplift in demand.
Contrast media agents	Updated as Visipaque 320 x100ml back in stock. Resupply date of remaining out of stock Omnipaque and Visipaque updated	See SPS shortage tracker

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Medication Safety Suite

Collaboration opportunities to improve medication safety

- Practical guidance on effective collaboration opportunities to promote medication safety improvements

Communication opportunities to improve medication safety

- Effective communication allows for timely responses to new and emerging medication risks and the sharing of potential safety solutions.

Responding to medication safety alerts and notifications

- Healthcare professionals responsible for medication safety in their organisation must deliver an appropriate response to safety alerts

Reporting and management of medication incidents and harms

- High quality reporting and management of incidents and harms ensures opportunities for learning and improving medication safety

Learning from medication incidents and harms

- Practical guidance to ensure opportunities to learn from local intelligence, including patient harm are translated into local and national learning

Understanding medication safety policy and frameworks

- 15 December 2022 · HCPs delivering the medication safety agenda in their organisation require an understanding of national policy, frameworks and legislation

Using the Medication Safety Observatory effectively

- 15 December 2022 · Effective use provides assurance that an organisation is aware of the most critical medication safety related information, and acts to improve safety

Promoting medication incident reporting

- 15 December 2022 · Increased medication incident reporting provides greater opportunities for learning and improving medication safety

Conducting a medication incident investigation

- 15 December 2022 · Practical guidance to support those undertaking medication incident investigations

Resources to support learning from medication incidents and harms

- 15 December 2022 · Organisations should utilise resources to effectively drive improvement based on the learning from incidents, concerns, disputes and claims

Practice support for the Medication Safety Officer (MSO)

- 15 December 2022 · An infrastructure of support opportunities exists that MSOs should utilise to deliver their role most effectively

The Medication Safety Officer (MSO) role

- 15 December 2022 · Understanding the role and responsibilities of the MSO in practice will assist organisations in delivering their medication safety agenda

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Assessing the impact of renal impairment on medicines safety in adults

- This article, part of a series on renal impairment and supported by information resources, provides advice on the considerations needed to assess renal function and ensure the safe use of medicines in the context of preserving kidney function.

Accessing resources for patients on high risk medicines

- A number of resources are available to support the safe use of high-risk medicines. HCPs should ensure they are available for their patients. NHS England resources for anticoagulants, lithium, methotrexate and steroids are featured.

SPS Spotlight Monthly Digest

- A slide deck summarising SPS outputs and resources. It should be distributed to relevant healthcare professionals and their teams.

Switching between gabapentin and pregabalin for neuropathic pain

- An overview of dose equivalences, switching methods and considerations to make before switching in adults with neuropathic pain.

Drug interactions: useful resources to support answering questions

- Our suggested resources can help primary care healthcare professionals find information to answer questions about drug interactions

Using codeine, dihydrocodeine or tramadol during breastfeeding

- Tramadol and dihydrocodeine can be used while breastfeeding for pain control. Codeine should not be used .

Switching between imatinib preparations

- Support for decision making when considering switching imatinib preparations including a locally adaptable patient information leaflet.

Using solid oral dosage form antibiotics in children

- Crushing or dispersing whole solid dosage forms or opening capsules is an "off-label" use. This includes use for Group A streptococcal infections.

Medication Safety in Primary Care: an on the couch conversation

- Tony Jamieson, National Clinical Improvement Lead, discussed medication safety issues with primary care pharmacy staff.

Specialist Pharmacy Service MHRA NHS England

National guidance, publications and resources

Concern over potential overuse following rapid increase in melatonin prescriptions for children and young people in England to treat sleep problems

- Analysis of NHS data obtained under FOI shows 56,002 unique patients aged ≤17 years were prescribed melatonin in Apr 2022 vs. 20,881 in Apr 2015, an increase of 168%. Number of patients aged 0–17 years prescribed melatonin hit more than 60,000 for first time in March 2022.
  - Source: Pharmaceutical Journal

Association of In Utero Antipsychotic Medication Exposure With Risk of Congenital Malformations in Nordic Countries and the US

- In cohort study (n>26 000; 6 countries), prenatal exposure was generally not linked to increase in risk of major congenital malformations. Observed increased risks of oral clefts with olanzapine, gastroschisis & other specific brain anomalies with atypicals, requires confirmation
  - Source: JAMA Psychiatry

Effectiveness of organisational interventions on appropriate opioid prescribing for non-cancer pain upon hospital discharge: A systematic review

- Review of 43 studies found guideline implementation, prescriber education & default opioid prescribing quantity changes appear effective to improve opioid prescribing on D/C. However, extent of reduction after multifaceted intervention strategies appear similar to simpler ones.
  - Source: British Journal of Clinical Pharmacology

National guidance, publications and resources

DTB select: Safety update: dupilumab and ocular adverse reactions

- Summary and context is provided for MHRA warning about the risks of ocular reactions to dupilumab and the need for a prompt review of new onset or worsening ocular symptoms.
    - Source: Drug and Therapeutics Bulletin

DTB select: Safety warning - combination products containing codeine and ibuprofen

- Article discusses new safety measures for codeine/ibuprofen combination products, recommended by the European PRAC, following a review of cases of toxicity associated with their abuse and dependence. It is not known if the MHRA will issue similar guidance in the UK.
    - Source: Drug and Therapeutics Bulletin

DTB Select: Risk of serious adverse effects with Janus kinase inhibitors

- Summary and context provided on EMA review into safety of abrocitinib, baricitinib, filgotinib, tofacitinib and upadacitinib, and recommended new measures to reduce the risk of serious adverse effects (cardiovascular problems, cancer, VTE and serious infections).
    - Source: Drug and Therapeutics Bulletin

Asthma patient information leaflets

- In partnership with Oxford Academic Health Science Network, the Accelerated Access Collaborative has produced three patient information leaflets covering having biologicals at home, informed conversations and getting the most from their medicines.
    - Source: Oxford Academic Health Science Network

National guidance, publications and resources

Rhabdomyolysis in a male adolescent associated with monotherapy of fluvoxamine

- Article describes a case report of rhabdomyolysis in a patient taking fluvoxamine for OCD. The symptoms were immediately reversed after the medicine was changed to sertraline. Authors note it is the first reported case of fluvoxamine-associated rhabdomyolysis.
    - Source: European Journal of Hospital Pharmacy

Republished case report: A probable case of collapse due to hyoscine patch

- Article reviews case of patient presenting with a fall & subsequent long lie, with profound confusion, slurred speech, expressive dysphasia, delirium, tremors, agitation & dehydration. Majority of symptoms were likely due to a hyoscine patch & improved markedly after its removal.
    - Source: Drug and Therapeutics Bulletin

Republished case report: Nitrofurantoin-induced agranulocytosis

- Article reviews report of a patient presenting with agranulocytosis following treatment with nitrofurantoin. Extensive workup was unremarkable and complete blood count recovered completely following its discontinuation. The case stresses the importance of monitoring treatments.
    - Source: Drug and Therapeutics Bulletin

Foreign Agencies

FDA investigating risk of severe hypocalcaemia in patients on dialysis receiving osteoporosis medicine Prolia (denosumab)

- Review of interim results from ongoing safety study suggests an increased risk of hypocalcaemia in patients with advanced kidney disease. Preliminary results from separate internal FDA study show a substantial risk with serious outcomes, including hospitalisation and death.

Australia to lose agency dedicated to better quality medicine use

- After ~25years, Australia's National Prescribing Service "NPS MedicinesWise" will close due to loss of government funding. Editorial notes with ~250,000admissions/year due to medicines, government appears poised to destroy an internationally well-respected, high-quality & effective pillar of support.

The impact of reorganising NHS services on patient safety

- An overview of incidents investigated by Healthcare Safety Investigation Branch (HSIB) in which service reorganisation has impacted adversely on patient safety. The authors provide a short list of positive actions that can be taken to help mitigate against those risks.

Material Regulation 28 – to prevent future deaths

Ref: 2022-0380

- Patient was admitted to an acute mental health ward. 3 days after their admission they were seen to be acting in a suspicious manner and gained access to the medicine room twice in the early hours. Upon being found in the medicine room, there was a failure to escalate risk to relevant persons. Multiple policies and practices were not followed adequately including
- Later that day they were found unresponsive in his room. CPR was commenced by staff however they were pronounced dead at the scene. At post mortem, a split plastic bag, containing 2 in addition to other tablets of shape, colour and size which were unidentifiable, were found in patient's rectum.

Cause of death

- Central Nervous System and Respiratory Depression
- Combined Drug Toxicity
- Misadventure and Neglect contributed to the cause of death.

MATTERS OF CONCERN:

- Evidence was heard that medication is kept in a locked room and in locked cabinets, in accordance with legislation. However, there is no record kept as to what medication is stored and how much.
- On a patient accessing medication, there is no knowledge as to whether anything has been taken and if so, how much, thereby limiting knowledge as to what treatment is to be considered and what action to be taken.

Material Regulation 28 – to prevent future deaths

Ref: 2022-0395

- Patient was found died at her home address after taking an excessive quantity of some of her prescribed medication.
- This patient's medication was required to be kept in a locked box due to a risk of her not taking the correct amount or taking too much medication.

Cause of death

- Drug related

MATTERS OF CONCERN:

- Despite this identified risk staff left regularly a nomad box containing a week's worth of medication unsecured in her kitchen cupboard.
- On the digital application used to inform carers of what medication to administer, which was used by the carers daily, there was no reference to keeping the medication in the secure box.